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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/071,751	02/07/2002	Shirley Wu Hunter	2618-17-C4-PUS-2	2578

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EXAMINER	
STEADMAN, DAVID J	

ART UNIT	PAPER NUMBER
1656	

DATE MAILED: 11/30/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/071,751	HUNTER ET AL.	
	Examiner	Art Unit	
	David J. Steadman	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 September 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *69-75* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *69-75* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

[1] Claims 69-75 are pending in the application.

[2] Applicant's amendment to the claims, filed 14 September 2006, is acknowledged. This listing of the claims replaces all prior versions and listings of the claims.

[3] Applicant's amendment to the specification, filed 14 September 2006, is acknowledged.

[4] Applicant's arguments filed on 14 September 2006 in response to the Office action mailed on 3 July 2006 have been fully considered and are deemed to be persuasive to overcome some of the rejections and/or objections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

[5] The text of those sections of Title 35 U.S. Code not included in the instant action can be found in a prior Office action.

Specification/Informalities

[6] In the prior Office action, it was noted that the substitute sequence listing filed 12 October 2005, replaced SEQ ID NO:61 and 62 such that they are identical to SEQ ID NO:61 and 62, respectively, of PCT/US97/05959 (*i.e.,* replacing A with T at nucleotide 329 of SEQ ID NO:61 and replace Ile with Asn at position 110 of SEQ ID NO:62). However, the substitute sequence listing filed 12 October 2005 failed to change the nucleotide sequence of SEQ ID NO:63 to correspond to the sequence of SEQ ID

NO:61. Since the original specification disclosed SEQ ID NO:63 as the complement of SEQ ID NO:61 (p. 94, lines 20-22), the examiner objected to the specification because SEQ ID NO:63 as filed on 12 October 2005 is not the complement of SEQ ID NO:61. The examiner interpreted this action as a mere oversight that would be corrected by a substitute sequence listing. Instead, the instant specification amendment deletes the disclosure of "[t]he complement of SEQ ID NO:61 is represented herein by SEQ ID NO:63." The amendment filed 14 September 2006 is objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure. 35 U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows. As noted above, the original application characterized SEQ ID NO:63 as being the complement of SEQ ID NO:61 (see particularly p. 94, lines 20-22). This relationship is supported by the sequences of SEQ ID NO:61 and 63 as originally filed, wherein SEQ ID NO:63 is the complement of SEQ ID NO:61. The original specification further discloses that SEQ ID NO:61 encodes SEQ ID NO:62, which is asserted to be a flea salivary protein (p. 94, lines 13-17). Thus, it follows that the complement of SEQ ID NO:63 encodes SEQ ID NO:62. The specification amendment filed 14 September 2006 to delete the disclosure that the complement of SEQ ID NO:61 is SEQ ID NO:63, breaks the disclosed complementary relationship such that SEQ ID NO:61 and SEQ ID NO:63 are no longer required to be interrelated and instead are independent nucleic acids. Further, by breaking this relationship, there is no requirement that the complement of SEQ ID NO:63 encodes SEQ ID NO:62, but encodes a polypeptide that is distinct from

SEQ ID NO:62. However, at the time of filing, there does not appear to be support in the original application for SEQ ID NO:61 being distinct from the complement of SEQ ID NO:63, nor does there appear to be support in the original application for the complement of SEQ ID NO:63 encoding a polypeptide other than SEQ ID NO:62.

Applicant is required to cancel the new matter in the reply to this Office Action.

Claim Rejections - 35 USC § 112, First Paragraph

[7] Claims 69-75 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

MPEP § 2163 states, "when filing an amendment an applicant should show support in the original disclosure for new or amended claims" and "[i]f the originally filed disclosure does not provide support for each claim limitation, or if an element which applicant describes as essential or critical is not claimed, a new or amended claim must be rejected under 35 U.S.C. 112, para. 1, as lacking adequate written description".

According to MPEP 2111.01.I, "[d]uring patent examination, the pending claims must be 'given their broadest reasonable interpretation consistent with the specification'" (emphasis added) and according to MPEP 2111.01.IV, "[w]here an explicit definition is provided by the applicant for a term, that definition will control interpretation of the term as it is used in the claim."

The original specification specifically defines SEQ ID NO:63 as the complement of SEQ ID NO:61 (p. 94, lines 20-22) and further specifically defines SEQ ID NO:61 as encoding SEQ ID NO:62 (p. 94, lines 13-17). As such, according to the specification, it necessarily follows that the complement of SEQ ID NO:63 encodes SEQ ID NO:62 and the examiner applied this interpretation in examining the claims. Thus, although the examiner acknowledged that the sequence of SEQ ID NO:63 is not the complement of SEQ ID NO:61 in the prior Office action, in view of the specification's limiting definitions (as noted above), SEQ ID NO:63 was interpreted as being the complement of SEQ ID NO:61 as listed in the sequence listing filed 12 October 2005 and the complement of SEQ ID NO:63 as listed in the sequence listing filed 12 October 2005 as encoding SEQ ID NO:62, which is disclosed as being a flea salivary protein (p. 94, second full paragraph). Because of the specific definitions as set forth in the specification, requiring that the complement of SEQ ID NO:63 encode the flea salivary protein of SEQ ID NO:62, a scope of enablement rejection as set forth below was not raised. However, the instant specification amendment breaks the originally disclosed relationship between SEQ ID NO:61, 62, and 63. As such, the specification no longer specifically defines SEQ ID NO:63 as the complement of SEQ ID NO:61 and no longer requires that the complement of SEQ ID NO:63 necessarily encodes SEQ ID NO:62. Thus, the specification amendment effectively alters and broadens the scope of polypeptides encompassed by the claims. The claims are rejected because the original application fails to support a polypeptide encoded by the complement of SEQ ID NO:63, wherein

the polypeptide is other than SEQ ID NO:62. Applicant is invited to show support in the application as filed for SEQ ID NO:63 encoding a polypeptide other than SEQ ID NO:62.

[8] Claims 69-75 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for SEQ ID NO:62, does not reasonably provide enablement for a polypeptide encoded by the full complement of SEQ ID NO:63. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

It is the examiner's position that undue experimentation is required for a skilled artisan to make and/or use the entire scope of the claimed invention. Factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands* (858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)) as follows: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure. See MPEP § 2164.01(a). MPEP 2164.04 states, "[w]hile the analysis and conclusion of a lack of enablement are based on the factors discussed in MPEP § 2164.01(a) and the evidence as a whole, it is not necessary to discuss each factor in the written enablement rejection" and that "[t]he language should focus on those factors, reasons, and evidence that lead the examiner to conclude that the

specification fails to teach how to make and use the claimed invention without undue experimentation, or that the scope of any enablement provided to one skilled in the art is not commensurate with the scope of protection sought by the claims." Accordingly, the Factors most relevant to the instant rejection are addressed in detail below.

The breadth of the claims: Claims 69 (claim 70 dependent therefrom) and 71 (claims 72-75 dependent therefrom) encompass a polypeptide that is SEQ ID NO:62 with a mismatch at position 110 changing Asn to Ile. The scope of claimed proteins is not commensurate with the enablement provided by the disclosure with regard to the the polypeptide that is encoded by the full complement of SEQ ID NO:63. In this case the disclosure is limited to the protein encoded by SEQ ID NO:61, *i.e.,* SEQ ID NO:62.

The state of the prior art; The level of one of ordinary skill; and The level of predictability in the art: At the time of the invention, methods for eliciting antibodies to a given antigen were well known in the prior art. However, it was highly unpredictable as to which alterations in a protein's amino acid sequence can be made with an expectation of maintaining the ability of an antibody to bind the altered polypeptide sequence. Put another way, it was highly unpredictable as to whether a mutant antigen, *i.e.,* a polypeptide encoded by SEQ ID NO:63, would generate an antibody that would bind to a known flea salivary antigen, *i.e.,* SEQ ID NO:62. This position is supported by the references of Abaza et al. (*J Protein Chem* 11:433-444) and Colman et al. (*Res Immun* 145:33-36), both cited in the Office action mailed 14 May 2004. Colman et al. teaches, "[s]ingle amino acid changes within the interface of an antibody-antigen complex... ...can effectively abolish the interaction entirely" (page 33, right column).

Also, a skilled artisan recognizes that the shape, *i.e.,* conformation, of a polypeptide is dependent upon its primary amino acid sequence and Abaza et al. teaches, "the reaction of a protein antigen with its antibodies is influenced by conformational changes" (page 436, left column, bottom to right column, top).

The amount of direction provided by the inventor and The existence of working examples: The specification provides only a single working example of the claimed protein, i.e., SEQ ID NO:62. This working example fails to provide an indication or expectation that the polypeptide encoded by SEQ ID NO:63 would elicit an antibody that binds SEQ ID NO:62. Further, the specification fails to provide guidance regarding those amino acids of SEQ ID NO:62 that may be altered by substitution, addition, insertion, and/or deletion with an expectation of maintaining the desired activity. Also, the specification fails to provide guidance as to how to use a polypeptide encoded by SEQ ID NO:63 that does not elicit antibodies to SEQ ID NO:62 or other flea saliva proteins.

In view of the scope of the claims, which encompasses a variant of SEQ ID NO:62, the lack of guidance and working examples provided in the specification, and the high level of unpredictability as evidenced by the prior art, it is the examiner's position that undue experimentation would be necessary for a skilled artisan to make and use the entire scope of the claimed invention. Applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re*

Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 102

[9] The rejection of claim 71 under 35 U.S.C. 102(b) as being anticipated by Sigma Chemical 1993 Catalog is withdrawn in view of the amendment to the claim to limit (b) to the amino acid sequence encoded by a nucleotide sequence that is the full complement of SEQ ID NO:63.

Conclusion

[10] Status of the claims:

Claims 69-75 are pending.

Claims 69-75 are rejected.

No claim is in condition for allowance.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Steadman whose telephone number is 571-272-0942. The examiner can normally be reached on Mon to Thurs and alternate Fri, 7:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

David J. Steadman, Ph.D.
Primary Examiner
Art Unit 1656